

## Current directions in the artificial heart program\*

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*The author reports his experimental and clinical experience in the development of an artificial heart. The major problems to be solved include: tissue interface, relative to the abnormal changes which occur in blood in contact with a foreign surface; a control mechanism to provide adequate stroke-volume to meet the needs of the body; materials which will last as long as possible and lastly the power or energy source of the device. The problem of interface seems to have been satisfactorily solved with the Dacron velour surface and the left ventricular by-pass pump has been used with success in the prolonged temporary assistance of failing hearts.*

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Tonight I would like to tell you about our experimental and clinical experiences in the development of a mechanical device to replace the pumping function of the heart. Obviously, the ultimate objective is to develop a mechanical device that will replace the total function of the heart — in other words, an artificial heart. But we have not yet reached that goal, so tonight I shall try to give you some idea of the present status of our research.

A number of problems must be solved, and we have learned enough to define and group them. The first — and the most important, perhaps — is related to the *tissue interface*, or *blood interface*. This is the contact surface of the blood when it moves from its normal environment within the blood vessels to an artificial one such as a mechanical pump. As long as the blood is in its normal habitat in the heart and blood vessels and is in contact with the normal intimal and endocardial surfaces, it undergoes no abnormal changes, but as soon as it comes in contact with a foreign surface of any kind, it undergoes certain changes. The longer the blood is in contact with this surface, the more severe the changes.

A second group of problems is related to the *control mechanism*, the mechanism to provide adequate stroke-volume, that is, to pump adequate blood with each beat to meet the needs of the body. The control mechanism ensures adequate minimum blood flow and adequate maximum blood flow. A critical aspect of this control, of course, is in the pumping action of the two sides of the heart. The normal heart, as you know, has two pumping chambers, the left and right ventricles, and the output of these is extremely well balanced normally. When the heart fails, however, the balance is disturbed. Indeed, this is one of the causes of heart

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failure. So one requirement of a mechanical pump is absolute coordination and balance of the two pumps. The control mechanism is therefore paramount.

A third group of problems is related to *materials*. Obviously, we want the materials used in a mechanical heart pump to last as long as possible. We must therefore guard against their undergoing temporal deterioration that would necessitate repair, for, like the heart itself, such a device must pump regularly and continuously, under all circumstances, for an indefinite period.

A fourth group of problems concerns the *power*, or *energy source*, of the device. Whether the energy source is implanted within the body or is carried outside the body, it must allow the patient to be completely ambulatory. Ideally, such a source of power would enable the patient to do almost anything he wished.

After years of reviewing these problems, we began laboratory investigation of them. The primary problem to be solved was the *interface*, since solutions to the other problems could not be applied to the pump until a satisfactory interface was found. We therefore realized that taking one step at a time would permit greater progress than attempting to solve the entire problem at one time. For this reason, we have concentrated on a limited aspect of the overall artificial heart problem — the development of a pump for temporary assisted circulation, for days, or perhaps weeks. Such a pump would represent a step toward the development of a pump for prolonged use.

We have observed that certain patients die in heart failure because when the pumping mechanism of the normal heart fails, we have no way to assist the circulation and keep the patient alive while the heart recovers and adequate cardiac output is restored. Cardiologists see patients of this kind with myocardial insufficiency or coronary arterial disease; some recover after having been in failure, whereas others do not. And in the operating room surgeons see patients whose cardiac output is fairly satisfactory when supported by the heart-lung machine, but who die from heart failure when this support is removed. On occasion, we observed that if we tried to

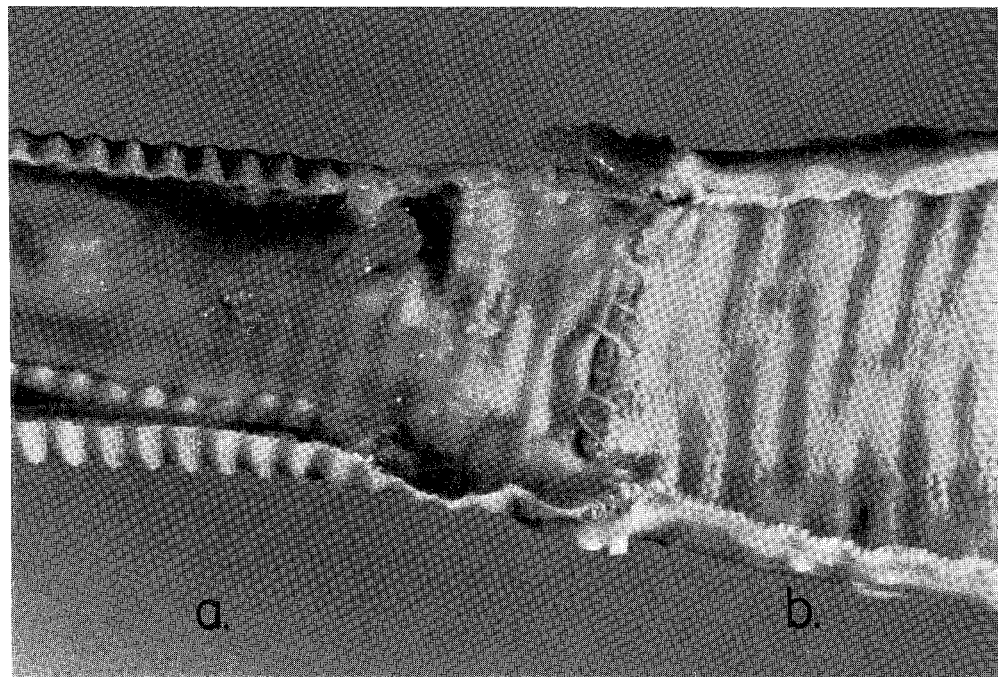


Fig. 1 - Photograph of opened arterial prosthesis used as femoral popliteal bypass graft, removed at operation two years after implantation. (a) Teflon portion of prosthesis, showing fibrinous clotted material not adherent to the fabric. (b) Dacron prosthesis that had been functioning for same length of time, completely covered with glistening, intimately adherent material that closely resembles natural intima.

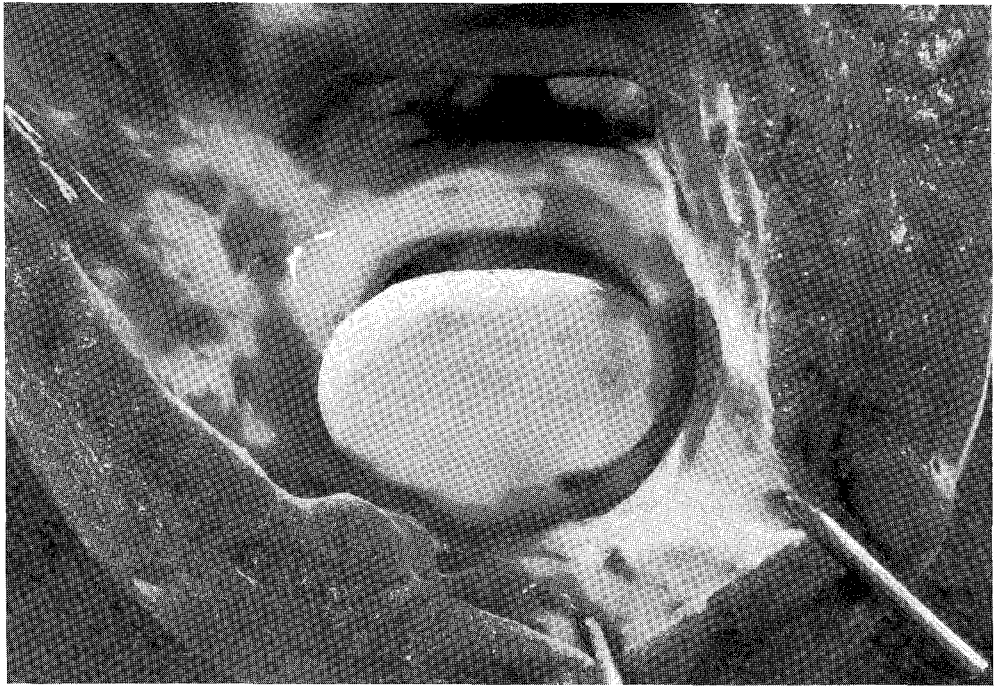


Fig. 2 - Experimental valve used to replace mitral valve in a calf, as the prosthesis appeared six weeks after operation (seen from ventricular side). Its surface, which is completely covered with Dacron velour, is now covered with newly formed pseudoendocardium.

discontinue use of the heart-lung machine suddenly, the heart would fail, but that if we resumed its use and assisted the heart for an hour or so more, discontinuing its use gradually, the heart would be able to take over. This experience provided evidence that, with a little longer support, the heart might recover. But we also observed that an hour or so is not always enough, and that support is sometimes needed for a longer period than the heart-lung machine can provide — sometimes days, or even weeks.

Now let me review a few aspects of these problems and of the application of the pump for temporary purposes.

### Interface problem

Blood pumped over a foreign surface, including any plastic material such as Silastic, will clot. This change can be expected whenever blood comes in contact with a surface other than its natural environment. This major problem must be completely resolved before we can develop an artificial heart. In our previous experience with artificial arteries, we had developed a surface similar to the normal intima of arteries. In figure 1, on the right side of the suture line, is a Dacron tube that has been functioning for about two years after implantation. On the left side is a Teflon tube that has been in place for the same amount of time. The difference in the two surfaces is evident. The surface of the Dacron prosthesis is completely covered with glistening material, or tissue, that is intimately adherent to it. By contrast, the Teflon portion of the prosthesis is covered with a fibrinous, somewhat clotted material that is not adherent to the fabric.

Dacron material that has been implanted for five years or longer is covered with a glistening, pale-white surface that closely resembles intima. Its thin appearance on cross-section indicates that it does not thicken with time. Histologic section shows the Dacron fibers to be completely surrounded by this fibrous tissue. The newly formed tissue makes a smooth intimal surface, completely adherent to the Dacron fibers in what might be regarded as the subintimal region. Indeed, in some instances small atheromas may be observed on this neointimal surface after several years. The experimental valve that we have used in animals is completely covered with Dacron velour. Such a valve, which had been implanted six weeks previously in

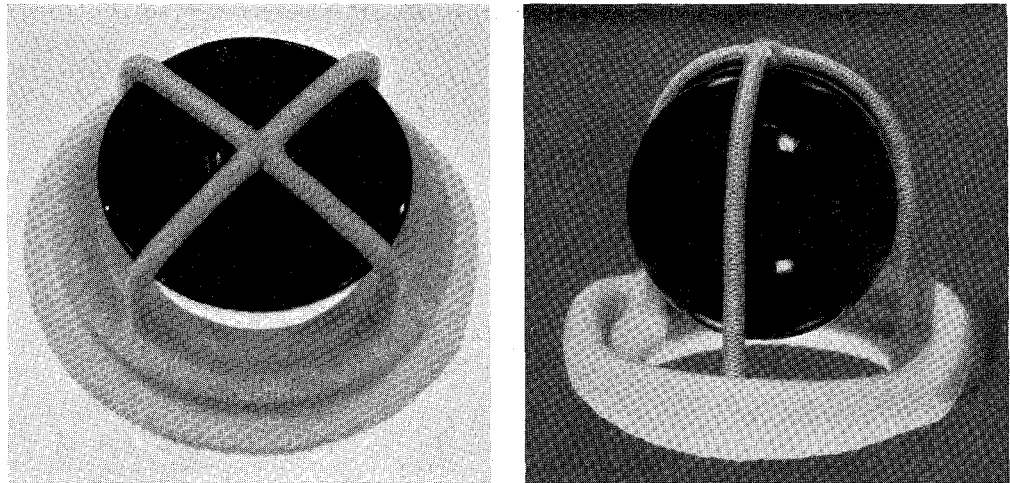


Fig. 3 - (a) Dacron velour-covered mitral disk valve. (b) Dacron velour-covered aortic ball valve.

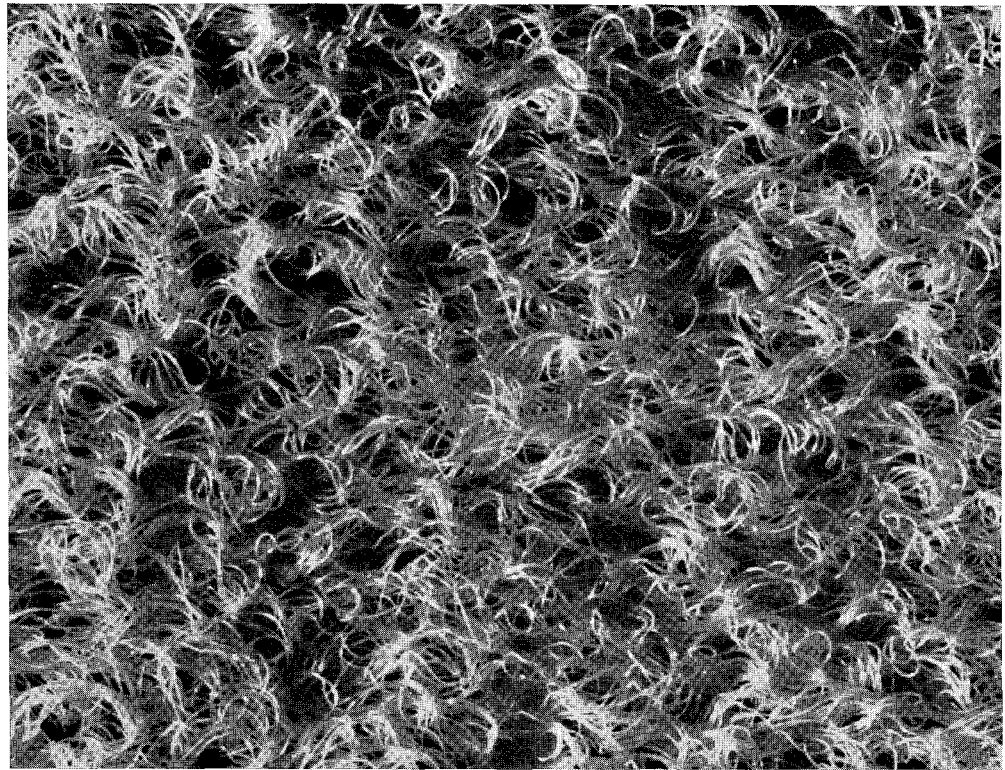


Fig. 4 - High-power photograph of Dacron velour lining used in left ventricular bypass pump. Blood becomes enmeshed with the loops of the fabric to form a new, intimately adherent surface that blood finds compatible.

a calf, is shown in figure 2. The lining looks very much like endocardium and completely covers the surface of the valve.

Figure 3 shows application of this principle of Dacron covering in development of new types of aortic and mitral valves which we are now using. Both the aortic and mitral valves are completely covered with Dacron velour to permit development of endocardium that will prevent formation of emboli on the valve.

These experiences and the knowledge acquired from use of artificial arteries led us to the creation of an interface of Dacron for our mechanical pump. We therefore first covered the lining of the entire pump with Dacron. Unlike the Dacron artery, however, which could be implanted in the body and would remain fixed while blood flowed across it, the mechanical pump required a mobile structure, in which the repeated to-and-fro motion of the diaphragm produced a certain

amount of breakage of the fibrinous elements adherent to it. For this reason, we turned to the Dacron velour surface (fig. 4). The fibrinous material laid down by the blood becomes enmeshed with the loops of the velour surface to create a new surface, and these loops tend to hold the fibrinous elements down firmly to the Dacron fabric. The fibrinous material deposited by the blood ultimately becomes well organized, creating a surface that blood finds compatible and will apparently tolerate.

In patients with left ventricular failure, the end-diastolic pressure and the mean left atrial pressure rise well above normal. We therefore need to remove this blood that the failing left ventricle cannot accommodate and that is causing the residual high pressure. If we could remove this blood from the left atrium and bring it to the systemic circulation by pumping it across and bypassing the left ventricle, we could relieve the left ventricle of that work load.

## Pumps

The various models of the pump that we developed are shown in figure 5. A version of the pump (fig. 5a) was implanted in a patient for the first time in 1963. It was attached to the left atrium and to the descending portion of the aorta. At that time, however, we were not lining the pump with Dacron velour, and after 48 hours of pumping, complications arose, in the form of thrombi and emboli. We have since circumvented this problem, at least partially. In fact, we are continually modifying all aspects of the design of these pumps to improve their efficiency and to make them approach more closely the pumping function of the natural ventricle. The most recent model of the pump is shown in figure 5f. The device is completely outside the body (fig. 6). One of its two connecting tubes is inserted into the left atrium through an intercostal incision, and the other to a systemic artery, such as the right axillary artery, through a small incision. We selected the right axillary artery because it is readily accessible and requires insertion of only one tube into the chest. We trigger the pump with the cycle of the electrocardiogram (fig. 7), so

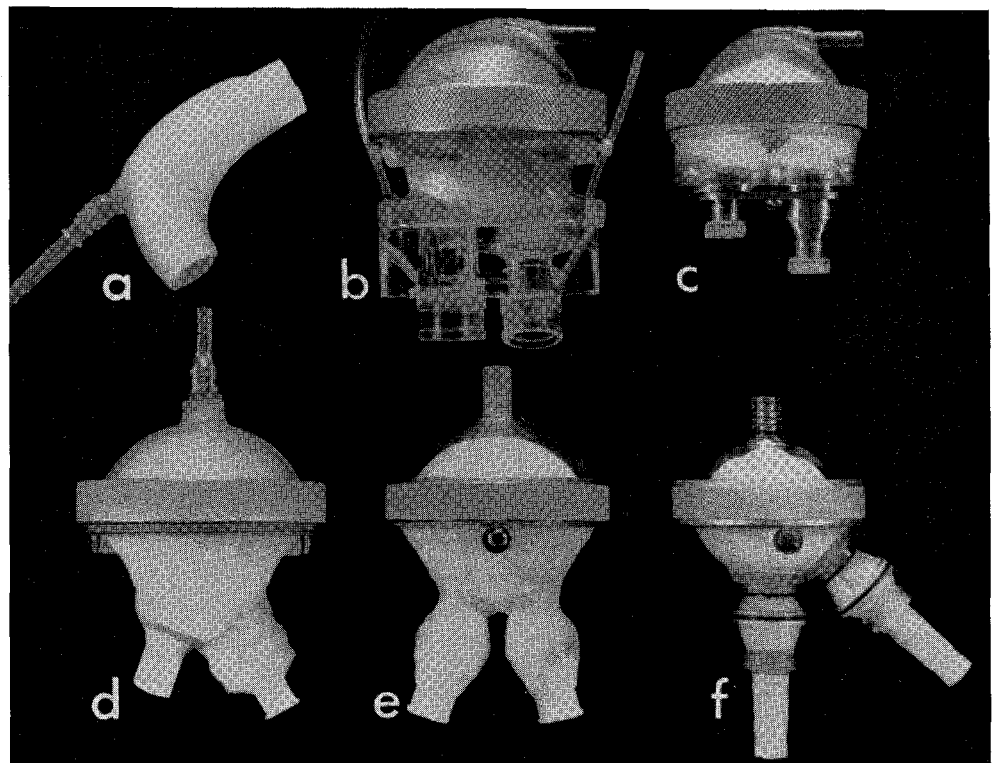


Fig. 5 - Six models of the left ventricular bypass pump. The pump shown in (a) was the first to be implanted in a patient, in 1963. The most recent model is shown in (f).

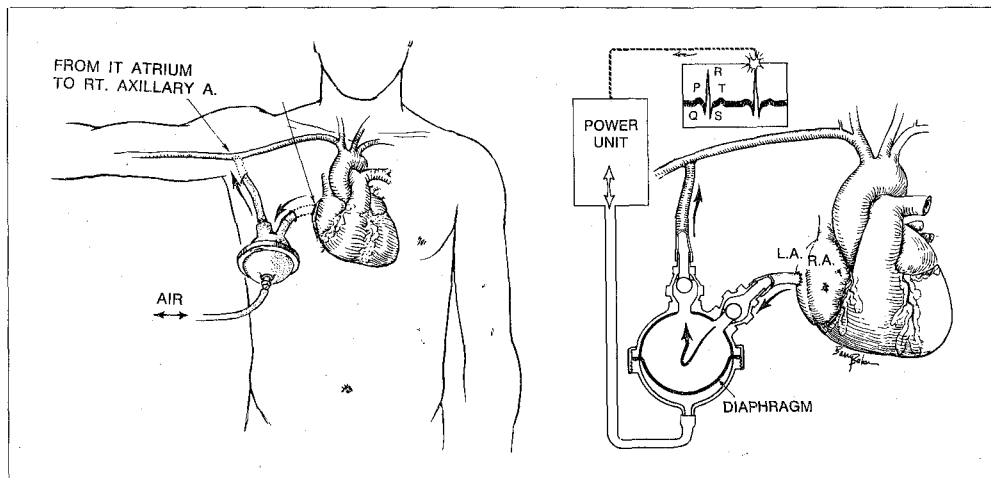


Fig. 6 - The left ventricular bypass pump is completely outside the body, one tube being inserted into the left atrium and the other into the right axillary artery.

Fig. 7 - The left ventricular bypass pump is triggered electrocardiographically, to pump blood during diastole, when the aortic valve is closed.

that the mechanical device pumps blood during diastole, when the aortic valve is closed.

Figure 8 shows the control mechanism in a recent model. After having used it for a while, we discovered ways of improving and refining it further, and we are now in the process of developing an entirely new mechanism.

#### Personal observations

In some patients, the heart-lung machine alone provides adequate circulatory assistance to the failing heart, as in the following case. The patient had severe aortic valvular disease, with preoperative signs of left ventricular failure and left atrial pressure of 45 mm Hg. The aortic valve was replaced by a prosthetic valve with use of cardiopulmonary bypass. At the end of the procedure, an attempt was made to discontinue use of the heart-lung machine. The left atrial pressure began to rise, but when extracorporeal circulation was resumed, it promptly fell to 10 mm Hg (fig. 9). After 15 minutes, an attempt was made to discontinue bypass, but the left atrial pressure promptly rose to 55 mm Hg. Cardiopulmonary bypass was resumed, at 3000 ml per min, and the left atrial pressure immediately fell. Another attempt was made to discontinue bypass, but left atrial pressure rose again. At this point it was decided to prolong the assisted circulation, in the hope that the heart might recover and be able to maintain adequate function. Accordingly, the bypass flow was gradually reduced during the next hour and a half, at the end of which time it was possible to discontinue use of the machine completely, with maintenance of adequate cardiac output.

In other patients, however, left atrial pressure has remained high despite prolonged circulatory assistance with the heart-lung machine. These patients require more prolonged support than can be provided by this apparatus, as exemplified by the following case in which we applied the left ventricular bypass pump. The patient was critically ill, with long-standing rheumatic heart disease and mitral insufficiency and with a preoperative left atrial pressure of 45 mm Hg. Replacement of the mitral valve required 40 minutes of use of total cardiopulmonary bypass at a rate of 3500 ml per min.

After operation, caval tourniquets were loosened to allow cardiac function to resume with use of only partial cardiopulmonary bypass. During the next twenty minutes the left atrial pressure fell to 25 mm Hg, and partial bypass was gradually decreased until it was stopped (fig. 10). Within five minutes, the left atrial pressure rose to 35 mm Hg, and the mean arterial pressure fell from 80 to 50 mm Hg. Within ten minutes after partial cardiopulmonary bypass was resumed, at a flow rate

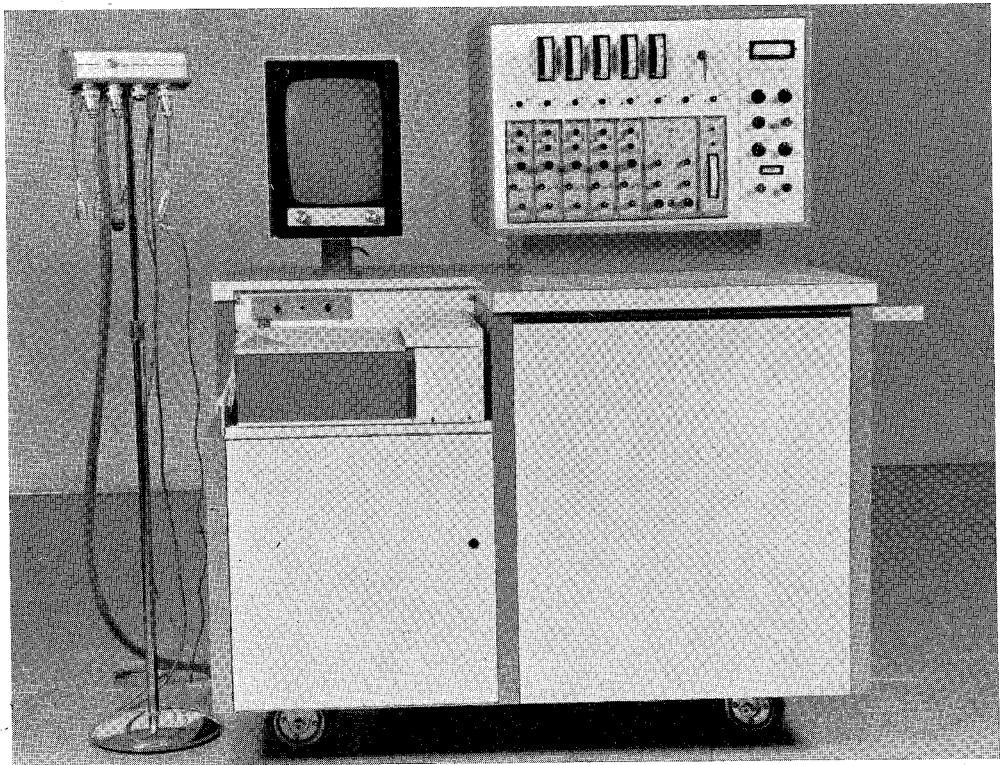


Fig. 8 - The control mechanism of a recent model of the left ventricular bypass model shown above has now been further refined.

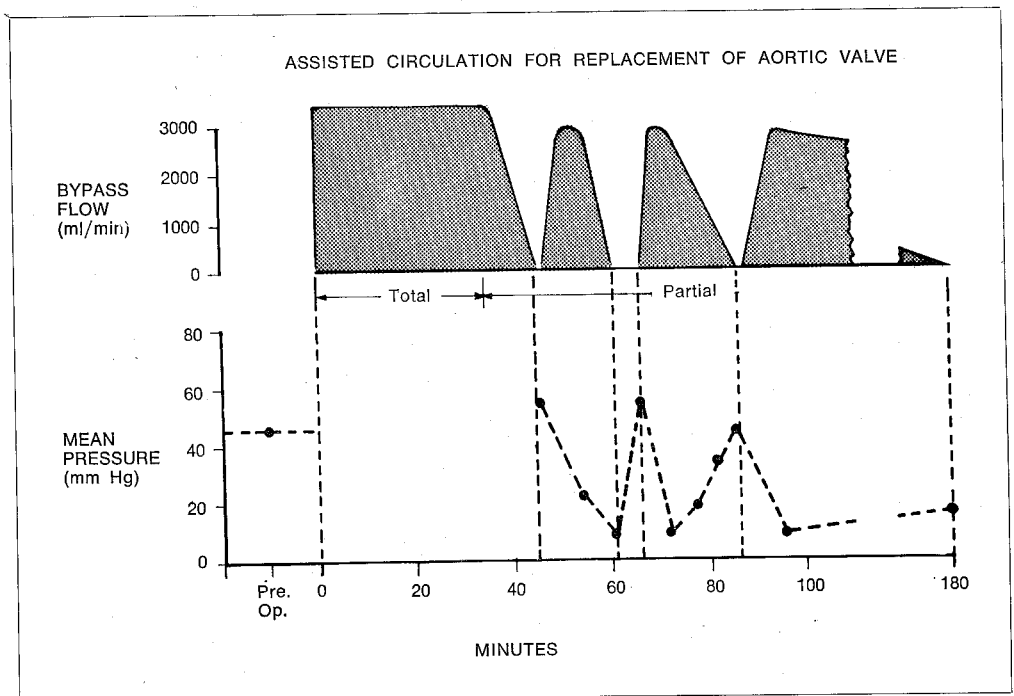


Fig. 9 - Effect of circulatory assistance by use for heart-lung machine after replacement of aortic valve. At end of operation, when discontinuance of extracorporeal circulation was attempted, left atrial pressure rose, but it fell to 10 mm Hg on resumption of partial cardiopulmonary bypass. Fifteen minutes later, when another attempt was made at discontinuance of bypass, the left atrial pressure rose to 55 mm Hg, then fell immediately when bypass was resumed at a flow of 3000 ml per min. A third attempt at discontinuance of bypass caused the left atrial pressure to rise once more. Resumption of bypass at 3000 ml per min, with gradual reduction in rate of flow during the next hour and a half, permitted complete discontinuance of bypass thereafter without a rise in left atrial pressure.

of 2500 ml per min, the left atrial pressure fell to 30 mm Hg and the mean arterial pressure increased to 70 mm Hg. Partial bypass was then gradually reduced to 800 ml per min, after which the left atrial pressure began to rise again and the arterial pressure to fall. It was therefore decided that more prolonged assisted circulation with use of the left ventricular bypass pump was necessary.

As partial cardiopulmonary bypass was gradually reduced during the next thirty minutes, the flow rate of the left ventricular bypass pump was accelerated until it reached 1200 ml per min. At this point, cardiac function appeared satisfactory. Mean arterial pressure was being maintained at 90 mm Hg, central venous pressure at 20 mm Hg, and left atrial pressure at 28 mm Hg. Cardiopulmonary bypass was discontinued. Vena caval and femoral arterial cannulas were removed, protamine was given to restore normal blood coagulation, and all incisions were closed.

Fifteen hours after operation, pump output was slowly reduced to 800 ml per min, and the left atrial pressure gradually rose from 22 to 26 mm Hg. When the pump output was increased to 1200 ml per min, however, the left atrial pressure promptly began to fall. Twenty-seven hours after operation, with left atrial pressure at 15 mm Hg, pump output was again slowly reduced to 800 ml per min, and this time left atrial pressure remained stable at a satisfactorily low level. Pump flow rate was gradually reduced until it reached 600 ml per min by the morning of the third day after operation. Left atrial pressure was stable at 7 mm Hg. Progressive reduction in flow rate of the pump caused no rise in left atrial pressure. On the fourth day after operation, the pump was turned off for six hours without any increase in left atrial pressure, and preparations were therefore made for its removal. The patient has completely recovered.

The left ventricular bypass pump has also been used in a thin, chronically ill patient with signs of severe aortic insufficiency and mitral stenosis. Cardiac catheterization confirmed the diagnosis of severe mitral insufficiency and aortic regurgitation, and

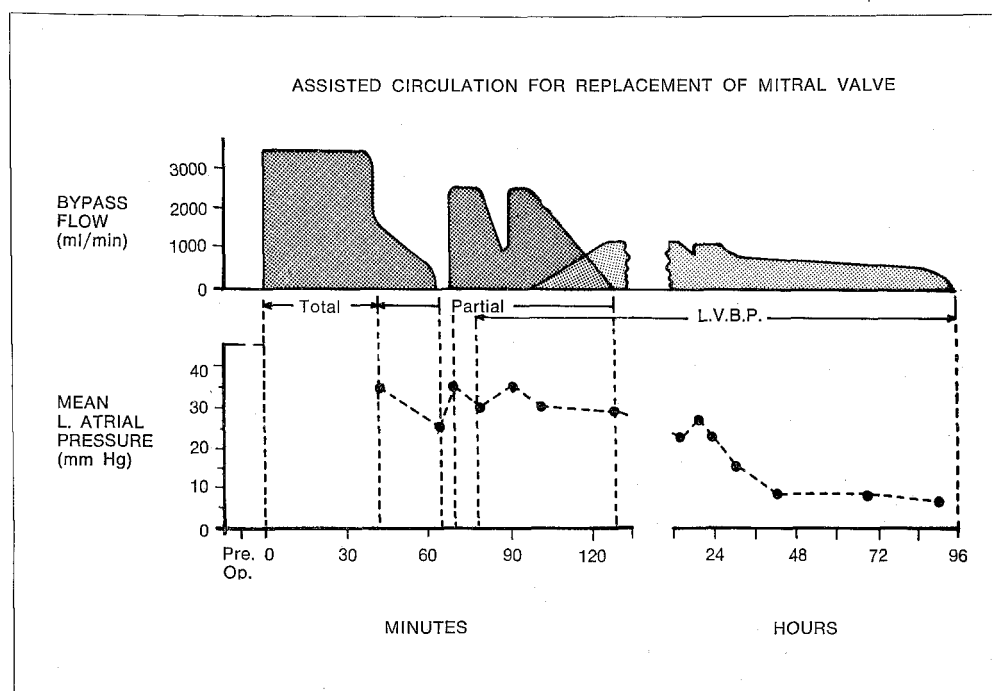


Fig. 10 - As indicated in the graph, after replacement of the mitral valve and attempt to discontinue cardiopulmonary bypass, left atrial pressure rose from 25 to 35 mm Hg. With resumption of partial cardiopulmonary bypass at 2500 ml per min, left atrial pressure decreased again. The left ventricular bypass pump was applied, and at a flow rate of 1200 ml per min, it was possible to discontinue cardiopulmonary bypass. Fifteen hours after operation, the pump output was slowly reduced from 1200 to 800 ml per min. Left atrial pressure gradually increased from 22 to 26 mm Hg. The pump output was again increased to 1200 ml per min, with immediate decrease in left atrial pressure.

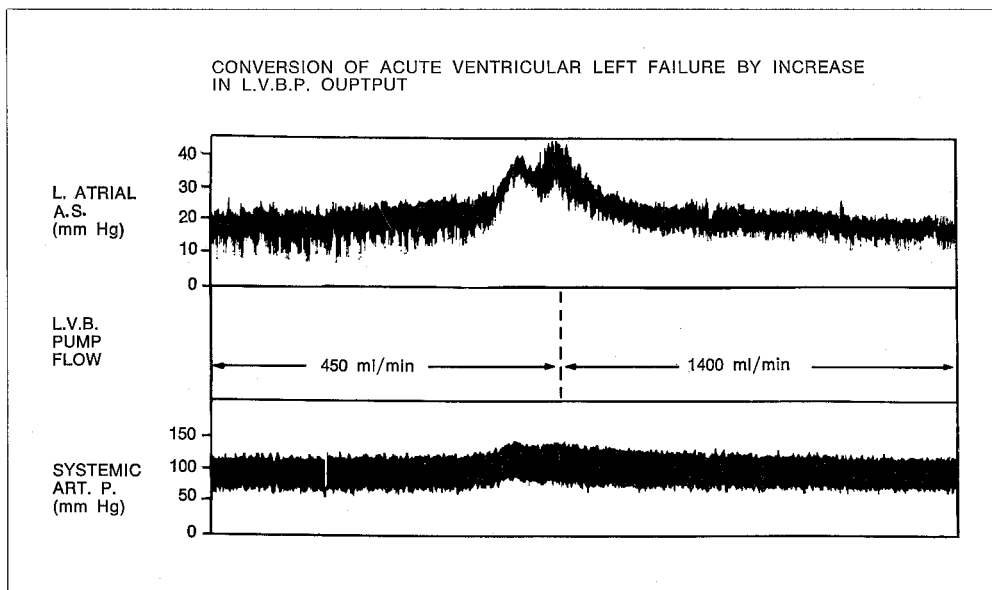


Fig. 11 - Effect of use of left ventricular bypass pump after replacement of aortic mitral valves. On the seventh day after operation, signs of acute pulmonary edema appeared. Left atrial pressure rose precipitously to 45 mm Hg, but when the outflow of the pump was increased from 450 to 1400 ml per min, it rapidly fell to about 15 mm Hg, and all signs of acute pulmonary edema disappeared.

indicated the need for replacement of aortic and mitral valves. Because of the high surgical risk involved, preparation was made for possible use of the left ventricular bypass pump.

After replacement of the valves, the high left atrial pressure persisted (35 mm Hg), and left ventricular end-diastolic pressure was 20 mm Hg. As partial cardiopulmonary bypass was gradually reduced during the next ten minutes, the flow rate of the left ventricular bypass pump was increased until it reached 1200 ml per minute. At this point, cardiac function appeared to be satisfactory; blood pressure was maintained at about 120/80 mm Hg, central venous pressure at about 12 mm Hg, left atrial pressure at 15 mm Hg, and systolic pulmonary arterial pressure at 40 mm Hg. Cardiopulmonary bypass was discontinued, and vena caval and femoral arterial cannulas were removed. Protamine was given to restore normal blood coagulation, and all incisions were closed.

On the third day after operation, the patient was progressing satisfactorily, with the pump output at about 800 ml per min. The flow was gradually reduced to 400 ml per min by the morning of the fourth day after operation. At noon on that day, however, systemic blood pressure began to fall progressively and left atrial pressure to rise moderately while urinary output decreased about 10 ml every 30 minutes. One milliliter of Mercuhydrin and 50 mg of Hydrodiuril were given, with no response after five hours. The outflow of the left ventricular bypass pump was then increased from 400 to 800 ml per minute, with immediate diuresis and restoration of left atrial pressure to normal. This improvement in renal function reflects the improvement in cardiac output effected by the left ventricular bypass pump.

On the seventh day after operation, after infusion of 500 ml of saline during renal function tests, left atrial pressure gradually rose during a period of about six hours. Rales in the chest developed, the patient began to cough pink, frothy sputum and became increasingly dyspneic, and signs of acute pulmonary edema rapidly developed. The left atrial pressure rose precipitously to 45 mm Hg. Within a few minutes after the left ventricular bypass pump outflow was increased from 450 to 1400 ml per min, the left atrial pressure began to fall, rapidly decreasing to about 15 mm Hg (fig. 11). Simultaneously, all signs of acute pulmonary edema disappeared, and the patient's condition improved strikingly. On the ninth day after

operation, the rate of flow was reduced to 350 ml per min, and roentgenograms of the chest showed the pulmonary fields to be clear and the size of the cardiac silhouette to be smaller. Progressive reduction in the pump's output caused no increase in left atrial pressure, and the pump was removed on the tenth day after operation.

Roentgenograms of the chest of this patient before and after operation provide a striking contrast (fig. 12). Before operation, the heart was grossly enlarged. The left ventricular bypass pump was used for ten days, after which the patient recovered completely. When she returned a little more than a year after operation, she was entirely asymptomatic. Catheterization data showed that before operation she had an extremely low cardiac output of 1.9 L per min, but that after operation it increased to 3 L per min. Hemodynamic studies showed that the mean wedge pressure of 38 mm Hg before operation had decreased to only 20 mm Hg six months later.

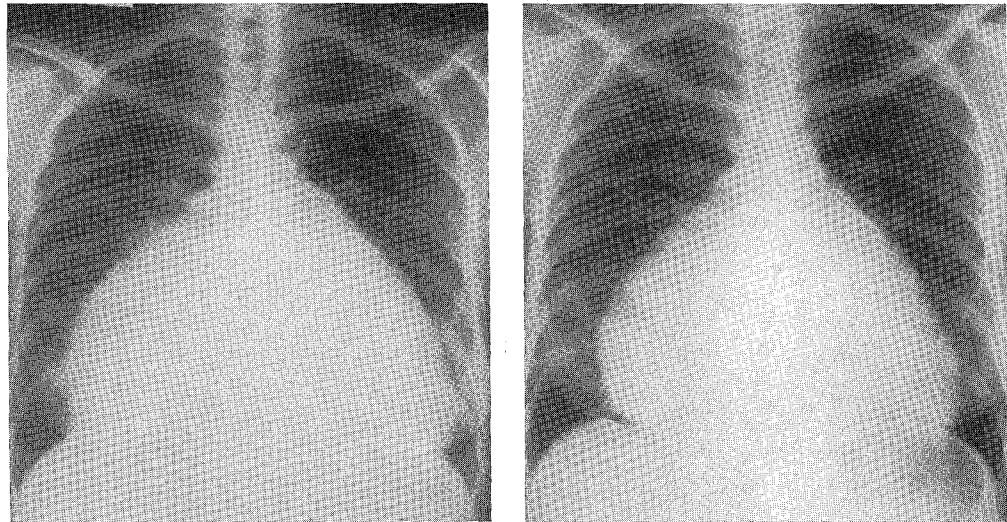


Fig. 12 - (a) Roentgenogram of the chest of a patient with severe rheumatic heart disease, causing aortic insufficiency and mitral stenosis. Before operation, the heart was grossly enlarged. The left ventricular bypass pump was used for ten days in this patient after the aortic and mitral valves had been replaced. (b) Roentgenogram of the chest of the same patient eighteen months after operation, showing notable reduction in size of the heart.

## Conclusions

In conclusion, I should like to summarize our approach to this research — first a definition of the problems as clearly as possible and then a search for their solutions, one at a time. I am sure that one question has arisen in your minds and that is: In the meantime, what about heart transplantation? Well, I believe that we should certainly move forward with this research as well, because solving the clinical problems at hand will require optimal use of all our current knowledge. But the clinical, ethical, logistic, and other problems associated with human cardiac transplantation point up the need to pursue development of an artificial heart all the more vigorously. One of the important differences, for example, between transplantation of a kidney and transplantation of the heart is the present availability of an artificial kidney that can sustain life should the transplanted kidney fail for reason of rejection or otherwise. We can keep such a patient alive for months, or even a year or longer, and can even transplant another kidney. But if we transplant a heart and that heart fails, then the patient's life is threatened because we do not have an artificial heart to sustain his life. This risk emphasizes the need for developing an artificial heart.

What are the prospects for development of an artificial heart? I think they are good. We know some of the problems, and have even defined them. Perhaps other

problems will arise as we gain more experience, but at least we know certain problems better now than we have ever known them before, and we are seeking solutions, but these obviously require considerably more research. Of course, the more people engaged in this research, the sooner will answers be found. Just as development of the heart-lung machine showed that cardiac function could be replaced, so development of the left ventricular bypass pump has shown that we can pump blood mechanically for days, or even weeks, in much the same ways as the normal heart and that a mechanical device can thus assume as much as half, or more, of the heart's function. If the artificial pump can function satisfactorily for a few days, then we should be able to extend its function for weeks, months, or even years. We simply need to solve the problems that arise with prolonged use, and these solutions will come with further research.

Finally, I want to express to you again my heartfelt thanks for your kindness, generosity, and warm hospitality.